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Original Research Article

Comparison of Efficacy of Ibuprofen & Paracetamol in the Treatment of Acute Migraine in Children – A Randomized Controlled Clinical

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Conflict of interest: Nil

Abstract

Background: Migraine is a common clinical condition in children affecting their quality of life. Limited literature studies are available on the pharmacological treatment of acute migraine in children. Thus, the present randomized controlled clinical blind trial was designed to evaluate the clinical efficacy of oral Ibuprofen with oral paracetamol in the acute treatment of migraine in children.

Material & Method: The study included 60 school going children (age 6-10yrs) fulfilling criteria of International Classification for headache disorders,3rd edition, with at least one migraine attacks per month for 2 hours; with recurrence for at least 6 months & with unsatisfactory relief from prior treatments. Written informed consent acquired from parents & permission undertaken by the ethical committee. Any other etiology of migraine attacks was ruled out. The cases were randomized into Group Ibuprofen (n=30) and Group Paracetamol (n=30). A written record was maintained at home. Pain relief (≥ 2-point reduction from the baseline values) & freedom from pain (VAS scale), associated symptoms, side effects of drugs were noted.

Results: No statistical differences in baseline characteristics found in the two groups. Pain relief in 95% of children and 33.3% reached freedom from pain at 2 hr interval with relief in associated symptoms in 50% of children. Relief after drug administration noted with regards to associated symptoms of nausea, vomiting, photophobia & phonophobia were observed with no statistically significant differences in both groups. Mild adverse events of epigastic pain & nausea reported in both groups.

Conclusion: Both Ibuprofen & Paracetamol are equally efficacious and can be adopted as safe, economical drugs in relieving the acute migraine in children.

Keywords: Migraine, Ibuprofen, Paracetamol, Children

Background

Pain is the most common reason requiring medical healthcare facilities. Migraine is very common disorder encountered in daily outdoor practice in paediatric patients. Its prevalence in children is around 8% in school going children which increases to 15% in adolescents. It is a type of disability hampering the academics & increasing absenteeism in children [1].

Chief complaints of the patients are recurrent throbbing headache lasting for few hours to a day. A mneumonic POUND

is used as a diagnostic aid for migraine identification where P stands for pulsatile quality of headache, O for one day duration (4-72hrs), U for unilateral location, N for nausea, vomiting and D for disability [2].

There can be other differential diagnosis for migraine like acute glaucoma, refractory errors, temporal arteritis, cluster headache etc. [2] Evidence suggests the use of various medications to treat acute migraine attacks . Mild to moderate cases can be using non-steroidal anti-inflammatory drugs (NSAIDS) and paracetamol. NSAIDS are drug of choice in acute migraine attacks .In a metaanalysis 200 mg & 400mg oral Ibuprofen doses were noted to be efficacious in relieving pain for short term with 24 hr freedom from pain as compared to placebo. The associated symptoms of photophobia & phonophobia were also relieved by 400mg dose [3]. Ketorolac iv usually used in hospital settings was observed to be effective in relieving headache one hr after iv administration [4].

In Severe cases or cases not responding to other treatments Triptans can be prescribed. Individual responses may vary & complete pain relief may not always be achieved [5]. In a metaanalysis conducted by Ferrari MD 2001 including 53 studies the most effective drugs were rizatriptan 10 mg (Maxalt),almotriptan(12.5mg) & eletriptan 80mg (Relpax) [6]. The dose of a particular drug should be increased before evaluating its response. Many clinical trials have observed that individuals not responding to one triptan may respond to another triptan [7]. The pharmacokinetics of each Triptan is different. Rizatriptan has a faster onset of action while eletriptan , naratriptan & frovatriptan have longer duration of action in comparison to sumatriptan .These drugs are readily available as dispersible tablets, nasal sprays and as subcutaneous administration [8]. A clinical trial by Dib M *et al* 2002 compared zolmitriptan & ketoprofen and concluded zolmitriptan to be more effective but also with more side effects of flushing & throat tightness [9].

Scarce studies are available in literature to provide a guidance to paediatricians in effective treatment of migraine attacks in children & adolescents [10]. Studies have observed ibuprofen, paracetamol, intranasal zolmitriptan & intranasal sumatriptan to be efficacious in management of acute migraine in paediatric patients [11]. Lewis DW conducted a systematic review & stated observed ibuprofen & paracetamol to be safe & effective drugs in children [12].

Thus the present randomized controlled clinical blind trial was thus undertaken to evaluate the clinical efficacy of oral Ibuprofen with oral paracetamol in the acute treatment of migraine in children.

Material & Methods

This blinded randomized controlled clinical study recruited 60 children (age 6-12 yrs) with the chief complaints of acute headache from September - Dec 2021 who came to the Department of Paediatrics at tertiary public health hospital in India. Children who fulfilled the criteria according to the International Classification for headache disorders,3rd edition (ICHD-3) who had at least one migraine attacks per month for 2 hours, with recurrence for at least 6 months & with unsatisfactory relief from prior treatments were included in the study . Children having any history of allergies of any kind, kidney, liver, or heart ailments, history of vomiting within half an hour of migraine, gastritis or acid peptic disease were excluded from the study. Proper investigations were carried out to rule out any other etiology of migraine attacks.

An Institutional ethical approval was undertaken before the start of the study. The nature of the study was explained to parents & written informed consent obtained.

After eligibility for inclusion was completed, patients underwent, ophthalmologic, neurologic & blood pressure assessment. The investigator recorded the socio-demographic characteristics, baseline values, family history & detailed headache history.

The 60 patients (male- 27; females 33) recruited were randomly allocated into two groups:

Group I: received oral Ibuprofen (10mg/kg/dose; n= 30 at home

Group P: received oral Paracetamol (15mg/kg/dose); n= 30 at home

The drugs were dispensed in a blinded manner, in opaque sealed envelopes.

The patients or their parents had to maintain a diary and record headache as none, mild, moderate & severe. Any other symptoms at the time of headache were noted down i.e. nausea, vomiting, photophobia, phonophobia). The patients had to administer the drug when the pain was moderate or severe. The drug could be repeated after 6-8 hrs, if headache persists.

The patients were enrolled for 5 weeks duration. The primary outcome measures were pain freedom (on a VAS scale) & Pain relief (≥ 2 point reduction from the baseline values) was noted 2 hrs after the study drug intake using 0-10 Visual Analogue Pain rating Scale, where 0 means no pain & 10 means extreme pain [13]. Adverse events after the drug intake were noted . Relief in any associated headache symptoms were noted down. After the study period was over the detailed headache charts were evaluated by the investigator.

Statistical Analysis

A minimum 30 patients were recruited in both groups to perform power calculations. Recorded data was tabulated & put to statistical analysis using SPSS software (Indian version). The statistical analysis involved chi square test & Wilcoxon test for two related samples. P Values less than 0.05 were considered significant.

Results

The baseline values were similar for the two groups.

Table 1: Baseline characteristics

Characteristics	Group Ibuprofen (n=30)	Group Paracetamol (n=30)	P value
Male /Female	13/17	14/16	>0.05
Age (mean ±SD)	8.9±1.58	9.62±1.46	>0.05
Duration of Headache(months)	11	12	>0.05
Episodes in last month	3	4	>0.05
Headache location			
Bilateral temporofrontal	17	18	>0.05
Unilateral temporofrontal	13	12	>0.05
Family History	6	8	>0.05
Associated symptoms			
Nausea	18	20	>0.05
Vomiting	8	15	>0.05
Photophobia /Phonophobia	24	27	>0.05

Discussion

The present clinical study recruited 60 school going children in age range of 6-12 yrs. The study noted pain relief in 95% of children and 33.3% reached freedom from pain at 2hr interval with relief in associated symptoms in 50% of children.

Table 2: Outcome Measures

Outcome	Group I (n=30) No. (%)	Group P (n=30) No. (%)	P value
Pain freedom	10 (33.33)	8(26.6)	>0.05
Pain relief	28(95)	26(86.6)	>0.05
No relief	2(6)	4	>0.05
Relief from Nausea	6(33)	8(36)	>0.05
Relief from Vomiting	4(50)	7(48)	>0.05
Relief from Photophobia/ Phonophobia	10(41)	7(27)	>0.05
Adverse events	n=5	n =2	>0.05
Epigastric pain	3(10)	1(6.6)	>0.05
Vomiting	2(6.6%)	1(3.3)	>0.05

The results are in accordance with study conducted by Evers 2006 comparing Ibuprofen with placebo drug in migraine attacks in children [14].Another hospital based, randomized cross over study involving 66 children, 4-16 yrs of age comparing Ibuprofen(10mg/kg) and acetaminophen (15mg/kg) & placebo. Complete pain relief at 2hr was 39% & 60% in acetaminophen & Ibuprofen group. At the end of 2 hrs, Ibuprofen was thrice more effective in migraine relief by two grades. The pain relief with Paracetamol is same as in this study but rates of relief with Ibuprofen are higher [15]. Other studies have observed superior analgesic potency of Ibuprofen in treatment of postoperative pain, fracture pain, fever, sprain etc [16-18]. Thus with a comparable gastrointestinal adverse events Ibuprofen is likely acceptable to be a first drug of choice in most acute pain condition in paediatric patients.

Evers & Lewis have observed Ibuprofen to be of superior analgesic potency than paracetamol on acute migraine attacks in paediatric patients [14] but in contrast Damen *et al* [19] meta-analysis did not found any significant differences in the efficacy of both drugs.

In the present study, associated symptoms of migraine i.e. nausea, vomiting, phonophobia, photophobia were reduced upto 40- 50%. Also epigastric pain was noted in 10% & 6.6% of Group I and Group P patients respectively. Adverse eve events of nausea repoted in 6.6% and 3.3% of Group I and Group P children respectively. There is a concern about the safety of analgesic use in paediatric patients. This is since the response of children to drugs varies due to differences in metabolism, pathophysiology, disease variants, pharmacodynamics, host response and adverse effects. Vries END *et al* 2008 in a systemic review reported 9% incidence rate of adverse events in hospitalized children [20]. Moreover, Drendall *et al* 2009 reported at least one adverse event in upto 30-50% cases when analgesic was used in children [21]. The American Academy of Paediatrics recommends use of Paracetamol, Ibuprofen & Opiods as drug of choice for treatment of acute pain in children [22]. Hartling *et al* 2016 reported NSAIDS & Paracetamol to be <10% associated rate of gastrointestinal symptoms [23]. Lesko *et al* 1999 [24], Perott DA *et al* 2004 [25] observed Paracetamol & Ibuprofen to have similar reported risk of nausea, vomiting, abdominal pain, cutaneous rashes. Study by Pavithra V *et al* reported NSAIDS & acetaminophen to be easily affordable therapeutic drugs for management of acute migraine in children. Evers *et al* 2006 in a study on treatment of childhood migraine by oral Ibuprofen(200mg,400mg) & oral Zolmitriptan (2.5mg) reported mild adverse events . Dizziness & somnolence in Zolmitriptan & gastrointestinal side effects in Oral Ibuprofen group were

noted. Although both drugs were considered safe [14].

Conclusion

Both Ibuprofen & Paracetamol are equally efficacious and can be adopted as safe, economical drugs in relieving the acute migraine in children.

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